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CANCER INCIDENCE AMONG WOMEN OF CHILDBEARING AGES EXPOSED TO TMI ACCIDENT RADIATION: 10-YEAR COHORT FOLLOW-UP*

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CANCER INCIDENCE AMONG WOMEN OF CHILDBEARING AGES EXPOSED TO TMI ACCIDENT RADIATION: 10-YEAR COHORT FOLLOW-UP

During the March, 1979 nuclear accident at Three Mile Island (TMI), residents in the vicinity of TMI were exposed to extra radiation(1,2) and experienced undue psychological stress(3) caused by fears associated with radiation. The accident radiation received by local residents came almost entirely from xenon gases and traces of radioactive iodine(4,5). The U. S. Nuclear Regulatory Commission estimated that the maximum wholebody gamma dose during the accident to anyone off-site was no greater than 100 millirems(4,5).

Shortly after the TMI accident, a special census was conducted of pregnant women within a 10-mile radius of TMI to determine the influence of the accident radiation and psychological stress on pregnancy outcome(6). For the purpose of comparison, another group of pregnant women was ascertained one year later within the same 10-mile area. A combined registry of these women has been updated for address and living status for future studies.

The study of cancer incidence reported in this paper is based on the combined group of registrants who were presumably exposed to the accident radiation, depending upon the location of residence and evacuation during the accident. In view of the prevailing uncertainty in low dose radiation carcinogenicity in humans(7) and the controversy regarding the amount of radioactive

releases during the accident, it seemed important to determine if the incidence of cancer was significantly elevated among those women who were exposed to the TMI accident radiation.

MATERIALS AND METHODS

Population At Risk:

The study cohort consists of 5,296 women of childbearing ages who were exposed to the TMI accident radiation and resided within a 10-mile radius. These women include 2,026 who were pregnant and 3,270 who were not pregnant at the time of the accident. The cohort was limited to those who had remained in Pennsylvania as of December 31, 1989, and considered for the study of cancer incidence reported here.

Through the registry update procedure, the size and age composition changed over time, but the "population at risk" or "person-years at risk" can be identified for any selected time period(8). For the present cancer study, "person-years at risk" for the 1982-89 period were used.

Cancer Incidence Data:

Incident cases of cancer within the study population diagnosed during the 7/1/82-12/31/89 period (7.5 years of observation with 10.8 years of follow-up) were identified through the Pennsylvania Cancer Registry(9), which was initiated in July, 1982. New cases of cancer which might have been diagnosed

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during the pre-Cancer Registry period (3/28/79-6/30/82) were not available, and not considered for this study.

For the purpose of the present study, all forms of cancer were considered together, as the number of cases reported was small. This was expected because the study population was relatively small in terms of "person-years" and is of childbearing ages when cancer risks are expected to be low.

Risk Factors and Potential Confounders:

The principal risk factor that may have had an impact on cancer incidence is radiation exposure from the nuclear accident. The estimated radiation exposure measurements used for the present study were individualized for those pregnant women residing within a 10-mile radius at the time of the accident(10). Both "maximum" and "likely" wholebody gamma doses were estimated from data on residence, evacuation, TLD and radioactive emissions and meteorological data. "Maximum" doses disregard evacuation, while "likely" doses take evacuation into account. The shielding factor was not considered.

Psychological stress, which was elevated during and after the TMI accident(3), may be a potentially important factor associated with cancer(11,12). In this study, physiological evidence of "psychological stress" was not measured. Instead, an indirect proxy measure was taken by asking women specific questions about the accident for which three mutually exclusive responses were available: "extremely disturbed", "somewhat

disturbed", or "not disturbed"(13). Such maternal characteristics as education, age, employment, medical history, pelvic x-rays, smoking and drinking were also used as potential confounders following stepwise regression analysis.

Data Analysis:

Data analysis included an ecological overview which examined the geographic difference in cancer incidence by quadrants. To determine if the incidence of cancer is significantly different from expectation or abnormal, an age-adjusted Standardized Incidence Ratio (SIR) was computed using SEER data as controls(14). SIR was tested for a statistical significance based on the Poisson model(15). Also used as "controls", were the TMI-area women of childbearing ages who were exposed to the 1979 accident radiation, but not pregnant at the time of the accident. This analysis was intended to examine the role of being pregnant in radiation carcinogenicity. Finally, the incidence of cancer was analyzed by the logistic regression model. In addition to accident radiation treated as the principal regressor, a number of potential confounders were simultaneously introduced into a regression model. Psychological stress was also considered in this analysis as a possibly important regressor.

RESULTS

Geographic Quadrants:

The total number of women of childbearing ages for ecological analysis was 5,296 who were distributed into four geographic quadrants(Table 1). Based on age-adjusted incidence rates, the risk of cancer was the highest (10.8 per 1,000 per 7.5 years) for the Southeast Quadrant and the lowest (5.5 per 1,000 per 7.5 years) for the Northwest Quadrant. The relative difference between these two extremes was statistically significant at the 5% level. However, this was contrary to levels of radiation exposure from the TMI accident.

Comparison With SEER Data:

To determine if the observed cancer incidence in the study population is abnormal, two reference populations were used. First, the 1981-85 SEER data(14) were applied to the study population (pregnant or not pregnant) of 5,292 women (36,888 person-years) to arrive at the expected number of cases (Indirect Method of Standardization). As shown in Table 2, the expected number of cancers during a 7.5 year period was 35.6 as compared with the number observed, 35 (SIR=0.98). Second, when analysis was limited to those who were pregnant at the time of the accident, the observed number of cancer was 15 as compared with 13.5 expected(Table 3). None of these differences were statistically significant.

Pregnant and Not-Pregnant Compared:

In order to determine if pregnancy status at radiation exposure plays a role in carcinogenesis, the incidence of cancer in the radiation-exposed and pregnant group was compared with that among those who were radiation-exposed but not pregnant. The result of this analysis is presented in Table 4. The age-adjusted expected number of cancer in the exposed and pregnant group was 12.2. as compared with 15, the number observed. The SIR, 1.23, indicates that the cancer risk in the exposed and pregnant group was 23% greater than expected, but this ratio was not statistically significant.

Multivariate Logistic Regression Analysis:

In the multivariate analysis, radiation and psychological stress as well as potential confounders were taken into account simultaneously. The results of this analysis are presented in Table 5. This analysis was limited to those who were pregnant at the time of the accident, for whom individualized radiation exposure measures were available.

As shown in Table 5, neither "maximum" nor "likely" wholebody gamma doses was significantly correlated to the incidence of cancer in the study population. The only potentially important finding is that those who were pregnant and took "extra medications"(such as tranquilizers, sedatives, and analgesics) to deal with anxiety during and after the accident had an increased risk of cancer (P=0.06).

DISCUSSION

This is a cohort follow-up study of cancer incidence within a relatively small, but well defined female population of childbearing ages, which has been followed for the past 10.8 years.

No clear evidence was found that the incidence of cancer was rising in the radiation-exposed cohort of women of childbearing ages since the TMI accident. Although the possibility that some cancer cases may have been under-reported (because data for the three years immediately following the accident were not available) can not be ruled out completely, missing cases, if any, are unlikely to be related to the TMI accident as most cancers(except leukemia) require a much longer latency period. A review of histological characteristics and organ sites affected did not show any sign of predominant radiation-sensitive malignancies. However, firm conclusions may not be made, at this time, primarily because most malignancies(except leukemia) would require a longer latency period.

Overall, the results of the study presented here do not provide evidence that TMI accident radiation releases influenced cancer risk among women of childbearing ages during the 10.8 years of follow-up. If any excess cancer risk was, in fact, present within the "exposed" population, it was either too small to be detected by the method used or not enough years have elapsed since the accident for most malignancies to develop.

Proxy measures of stress were not associated with cancer incidence. However, elevated risks of cancer, at the border line significance, in relation to "extra medication" to deal with anxiety may need further evaluation.

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Table 1. Comparison of Crude and Age-Adjusted Cancer Incidence Rates among Women of Childbearing Ages by Four TMI-Radius Geographic Quadrants: 7/1/82-12/31/89 (7.5-Year) Period

Geographic Quadrant (Mean Wholebody Gamma Dose: Maximum)	Female Pop. at Risk (1979)	Cancer Incidence (7.5-Years) Obs. No. (in Quad.)	Cancer Incidence (7.5-Years) Crude Rate/ 1,000	Exp. No. of Cancers in 7.5 Yrs. in Stand. Pop.	Age-Adjusted Rate/ 1,000/ 7.5 Yrs.	95% CI
Northeast (10 mrem)	1,150	10	8.70	42.4	8.01	5.60-10.42
Southeast (3 mrem)	613	7	11.42	57.2	10.80	8.00-13.60
Southwest (6 mrem)	702	3	4.27	34.7	6.55	4.37-8.73
Northwest (11 mrem)	2,831	15	5.30	29.0	5.48	3.49-7.47

Notes: This Cohort represents women of childbearing ages who lived in a 10-mile radius around the TMI nuclear power plant at the time of the accident (3/28/79).

Cancers analyzed here cover those which occurred during the 7/1/82-12/31/89 (7.5-year) period. (Cancer Registry for this area was initiated July 1, 1982.)

Total (combined) 10-mile radius female population (5,296), as of 1979, was used as the "standard" (Direct Method of Standardization) to calculate the expected number and age-adjusted cancer incidence rate for each geographic quadrant.

CI = confidence interval.

Table 2. Calculation of the Expected Numbers of Incident Cancer Cases for the 7/1/82-12/31/89 (7.5-Year) Period among Women of Childbearing Ages, Then Living in a 10-Mile Radius around TMI, by Application of SEER Females as Controls

	Control: SEER Females (1981-85)	Women in a 10-Mile Radius (Accident Radiation-Exposed)				
Age Groups	Proportion (Risk) of Cancers (5-Yr. Average Annual)	No. of Persons (as of 1982)	Aver. Pers. Years at Risk (1982-88)	Obs. No. of Cancers in 7.5 Yrs.	Exp. No. of Cancers in 7.5 Yrs.	Ratio (Obs./ Exp.)
15-19	.000184	154	240	0	0.0	-0-
20-24	.000275	1210	3943	2	1.1	1.82
25-29	.000520	1891	10478	6	5.4	1.11
30-34	.000912	1504	12584	11	11.5	0.96
35-39	.001559	451	7382	10	11.5	0.87
40-44	.002523	72	1950	6	4.9	1.22
45-49	.003926	10	311	0	1.2	-0-
Total	.....	5292	36888	35	35.6	0.98

Notes: Control population = SEER females; 1981-85 (5-year) occurrences.

Study population represents women of childbearing ages who lived in a 10-mile radius around the TMI nuclear power plant at the time of the accident (3/28/79).

Observed numbers of cancers cover those which occurred during the 7/1/82-12/31/89 (7.5-year) period. (Cancer Registry for this area was initiated July 1, 1982.)

Expected numbers were calculated by application of the age-specific cancer incidence rates for the Control Population.

Reference: H. Kahn. "An Introduction of Epidemiologic Methods". Oxford Univ. Press, 1983. Pp. 146-160.

Table 3. Calculation of the Expected Numbers of Incident Cancer Cases for the 7/1/82-12/31/89 (7.5-Year) Period among Women of Childbearing Ages, Exposed to Accident Radiation While Pregnant and Living in a 10-Mile Radius around TMI, by Application of SEER Females as Controls

	Control: SEER Females (1981-85)	Radiation-Exposed and Pregnant Women				
Age Groups	Proportion (Risk) of Cancers (5-Yr. Average Annual)	No. of Persons (as of 1982)	Aver. Pers. Years at Risk (1982-88)	Obs. No. of Cancers in 7.5 Yrs.	Exp. No. of Cancers in 7.5 Yrs.	Ratio (Obs./ Exp.)
15-19	.000184	66	107	0	0.0	-0-
20-24	.000275	430	1407	1	0.4	2.50
25-29	.000520	787	4138	3	2.2	1.36
30-34	.000912	562	4962	4	4.5	0.89
35-39	.001559	157	2743	4	4.3	0.93
40-44	.002523	20	654	3	1.7	1.76
45-49	.003926	3	92	0	0.4	-0-
Total	.....	2025	14103	15	13.5	1.11

Notes: Control population = SEER females; 1981-85 (5-year) occurrences.

Study population represents women of childbearing ages, exposed to accident radiation while pregnant, who lived in a 10-mile radius around the TMI nuclear power plant at the time of the accident (3/28/79).

Observed numbers of cancers cover those which occurred during the 7/1/82-12/31/89 (7.5-year) period. (Cancer Registry for this area was initiated July 1, 1982.)

Expected numbers were calculated by application of the age-specific cancer incidence rates for the Control Population.

Reference: H. Kahn. "An Introduction of Epidemiologic Methods". Oxford Univ. Press, 1983. Pp. 146-160.

Table 4. Calculation of the Expected Numbers of Incident Cancer Cases for the 7/1/82-12/31/89 (7.5-Year) Period among Women of Childbearing Ages, Exposed to Accident Radiation While Pregnant and Living in a 10-Mile Radius around TMI, by Application of Women of Childbearing Ages, Exposed to Accident Radiation But Not Pregnant, as Controls

	Control: Radiation-Exposed But Not Pregnant (N=3,267)	Radiation-Exposed and Pregnant				
Age Groups	Proportion (Risk) of Cancers (7.5-Yr.) Average Annual	No. of Persons (as of 1982)	Aver. Pers. Years at Risk (1982-88)	Obs. No. of Cancers in 7.5 Yrs.	Exp. No. of Cancers in 7.5 Yrs.	Ratio (Obs./ Exp.)
15-19	.000000	66	107	0	0.0	-0-
20-24	.000394	430	1407	1	0.6	1.67
25-29	.000473	787	4138	3	2.0	1.50
30-34	.000918	562	4962	4	4.6	0.87
35-39	.001293	156	2743	4	3.5	1.14
40-44	.002315	20	654	3	1.5	2.00
45-49	.000000	3	92	0	0.0	-0-
Total	.....	2025	14103	15	12.2	1.23

Notes: Control population represents women of childbearing ages, exposed to accident radiation, but not pregnant, who lived in a 10-mile radius around the TMI nuclear power plant at the time of the accident (3/28/79).

Study population represents women of childbearing ages, exposed to accident radiation while pregnant, who lived in a 10-mile radius around the TMI nuclear power plant at the time of the accident (3/28/79).

Cancers analyzed here cover those which occurred during the 7/1/82-12/31/89 (7.5-year) period. (Cancer Registry for this area was initiated July 1, 1982.)

Expected numbers were calculated by application of the age-specific cancer incidence rates for the Control Population.

Reference: H. Kahn. "An Introduction of Epidemiologic Methods". Oxford Univ. Press, 1983. Pp. 146-160.

Table 5. Multiple Logistic Regression Analysis of Cancer Incidence among Women of Childbearing Ages, Exposed to Accident Radiation While Pregnant, by 11 Risk Factors: 10-Mile Radius around TMI (N=2,026)

Risk Factors	Logistic Regression Coefficient	Standard Error	P
Education	-0.4296	0.5566	0.4402
Age	0.8045	0.5333	0.1314
Employment	0.4134	0.5723	0.4701
Medical history	-0.5139	0.5409	0.3421
Pelvic X-ray	0.0940	0.7752	0.9034
Smoking	-0.1178	0.5812	0.8394
Drinking	0.8028	0.6092	0.1875
Psychol. disturbance	-0.4725	0.6866	0.4913
Extra medication	1.5158	0.8164	0.0634
Maximum gamma dose	-0.0053	0.0098	0.5881
Likely gamma dose	0.0077	0.0216	0.7223

Notes: This Cohort represents women of childbearing ages, exposed to accident radiation while pregnant, who lived in a 10-mile radius around the TMI nuclear power plant at the time of the accident (3/28/79).

Excludes unknown data.